

REMARKS

Claims 9 and 29-32 have been canceled without prejudice. Claims 1 and 8 have been amended to more particularly point out the claimed subject matter. New claims 33-37 have been added to include a subset of genes as recited in original claim 1. Support for the claim amendments and new claims can be found throughout the specification (e.g., pages 12, lines 11-19; page 71, lines 17-19; and Table 1 on pages 79-81) and original claims (e.g., claims 1 and 9). No new matter has been introduced. Applicants submit that the amendments are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants note that the Examiner has withdrawn the previous rejections under 35 U.S.C. § 112, second paragraph and under 35 U.S.C. § 102(b) (citing Hillman et al.).

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Election/Restriction

The Office Action has acknowledged Applicants' election, with traverse, of Group I (claims 1-11) and the species election of mRNA in the Response filed on October 2, 2006.

Priority

The Office Action maintains that the claims presently have a priority date of January 29, 2002. Applicants reserve the right to traverse the Examiner's assertion until allowable subject matter is found; at which point, Applicants will provide supportive priority documents if deemed necessary.

Sequence Compliance

The Office Action asserts that the application fails to comply with the requirements of 37 CFR 1.821 (c) because the genes listed in Table 1 and claimed (independent claim 1) are considered essential material and should be included in a sequence listing. In response, Applicants submit herewith a revised Sequence Listing which includes the sequences as disclosed in the application (including those in Table 1). Applicants have also amended the specification (i.e., Table 1) solely to identify the sequences with SEQ ID NOs.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Solely to expedite prosecution, Applicants have amended certain claims. Such amendments are not made in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

a. The Examiner asserts that "Table 1 refers to the genes by accession number, gene name, chromosome location, and function. Thus, it is not clear if the genes of Table 1 requires a specific sequence, the entire gene sequences, a sequence associated with the accession number, a sequence associated with the gene name, an EST, etc." Solely for greater clarity, Applicants have amended claims 1 and 8 to identify the genes by including SEQ ID NOs, rendering the rejection moot.

The Examiner also asserts that "it is not clear from the claims if all the genes in Table 1 are required or only a subset of the genes of Table 1." In response, Applicants have amended independent claim 1 to clarify that the plurality of genes are at least 40 genes selected from SEQ ID NOs: 1-43. Dependent claim 8 has been amended to specify that the plurality of genes are set forth in SEQ ID NOs: 1-43.

b. The Examiner asserts that there is insufficient antecedent basis for the limitation "the plurality of genes" in claims 8 and 9. In response, Applicants have amended claim 8 and canceled claim 9 without prejudice, rendering the rejection moot.

In view of the above amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw all rejections under 35 U.S.C. 112, second paragraph.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, and 8-10 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action asserts that "[t]he claimed invention does not include any structural information regarding the genes of the test expression profile and refers to the genes of Table 1 via accession number, gene name, chromosome location, and function (i.e., sequences are not provided." Office Action, page 8, first paragraph.

As described above, Applicants have amended independent claim 1 to define the genes by including SEQ ID NOs. Claim 1 as amended recites a method for diagnosing an oral cancer in a patient, comprising: a) obtaining a biological sample from a patient; b) determining the expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile, wherein the plurality of genes are at least 40 genes selected from SEQ ID NOs: 1-43; and c) comparing the test expression profile with at least one signature expression profile from a patient known to have an oral cancer, wherein said signature expression profile consists of said plurality of genes and is indicative of an oral cancer, wherein if the test expression profile substantially matches said signature expression profile, the patient has the oral cancer.

Further, Applicants have added new claim 33 to recite a method for diagnosing an oral cancer in a patient, comprising: a) obtaining a biological sample from a patient; b) determining the

expression level of a plurality of genes associated with an oral cancer in the biological sample, thereby producing a test expression profile, wherein the plurality of genes consist of at least five genes selected from SEQ ID NOs: 3, 5, 10, 15, 16, 21, 22, 27, 28, 31, 32, 35, 37, and 40; and c) comparing the test expression profile with at least one signature expression profile from a patient known to have an oral cancer, wherein said signature expression profile consists of said plurality of genes and is indicative of an oral cancer, wherein if the test expression profile substantially matches said signature expression profile, the patient has the oral cancer.

The specification provides both working examples and sufficient descriptions of the method as recited in amended claim 1 and new claim 33 (see, e.g., working examples on pages 69-80). Applicants believe the claim amendments have obviated the written description rejection. One of skill in the art would readily appreciate that Applicants were in possession of the claimed invention at the time this application was filed in view of the teachings of the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections for lack of written description.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 5-6, and 8-11 are rejected for alleged lack of enablement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Examiner asserts that "[t]he present claims do not provide any structural limitations regarding the genes of the test expression profile and do not provide any structural information regarding the genes of Table 1. Table 1 refers to the genes by accession number, gene name, chromosome location, and function." Office Action, page 13, first paragraph.

As described above, independent claim 1 as amended relates to a specific subset of genes and the genes are clearly identified by SEQ ID NOs. Applicants believe the claim amendments have obviated this enablement rejection.

The Examiner further asserts that "[w]hile the presently claimed method is enabled for screening biological samples for gene expression, the intended use as a means for diagnosing oral cancer is not enabled . . . The specification does not provide information regarding the level of upregulation or downregulation compared to control (e.g. normal, noncancerous sample). Accordingly, the claims scope is unduly broad with respect to encompassed genes and expression profiles." Office Action, the paragraph bridging pages 13 and 14.

Applicants respectfully disagree. The specification is enabling for the full scope of the claimed invention. As described above, the specification provides working examples to show that all the genes in Table 1 were differently expressed in oral cancer patients. As such, one of skill in the art would know that the expression profile of a specific subset of the genes in Table 1 (e.g., claim 1 or 33) could be successfully used for diagnosis of an oral cancer. Moreover, the specification teaches how to measure the gene expression levels in a biological sample and how to compare the test expression profile with a signature expression profile from a patient known to have an oral cancer. Further, the level of skill in the art was high at the time of the filing date of the present application. In fact, the techniques involved in the invention, all of which were well known in the art even before the filing date, are highly reliable and can be readily practiced by a skilled artisan.

It is well settled that, "[I]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." (MPEP 2164.04).

In this case, the Examiner has not provided adequate reasoning to support the contention that the claims are not enabled for methods for diagnosing oral cancer. The Examiner has not provided any factors, reasons, or evidence to show that the instant claims, which the Examiner acknowledges are enabled for screening biological samples for gene expression, would not also be enabled for diagnosing oral cancer. Applicants submit that the Examiner has not met the burden of establishing a *prima facie* case of lack of enablement.

Applicants submit that the pending claims are enabled throughout their scope. Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 5-6, and 8-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that the term "signature expression profile" is indefinite.

Solely to expedite prosecution, Applicants have amended claim 1 to clarify that the signature expression profile is from a patient known to have an oral cancer and consists of at least 40 genes selected from SEQ ID NOs: 1-43, rendering the rejection moot.

Claim Rejections under 35 U.S.C. § 102(e)

Claims 1, 5-6, and 8-10 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Katz et al. (U.S. Patent No.6,797,471). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Katz et al. fail to satisfy the criteria for anticipating the present invention. Katz et al. describe use of gene probes for specific regions of chromosome 3 (3p21.3) and chromosome 10 (10q22) for diagnosis and prognosis of smoking related cancers. However, Katz et al. do **not** teach or suggest step (b) or (c) of claim 1, which involves a test expression profile and a signature expression profile of at least 40 genes selected from SEQ ID NOs: 1-43. In addition, Katz et al. do **not** teach or suggest step (b) or (c) of new claim 33, which involves a test expression profile and a signature expression profile of at least 5 genes selected from SEQ ID NOs: 3, 5, 10, 15, 16, 21, 22, 27, 28, 31, 32, 35, 37, and 40.

Accordingly, Katz et al. do not teach all the elements of independent claim 1 or 33 and fail to anticipate claim 1 or 33. For the same reasons, Applicants submit that all claims depending from claim 1 or 33 are not anticipated by Katz et al. In view of the above amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

Claim Rejections under 35 U.S.C. § 102(e)

Claims 1, 5-6, and 8-10 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Warrington et al. (U.S. Patent No. 7,108,969). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Applicants contend that Warrington et al. fail to satisfy the criteria for anticipating the present invention. Warrington et al. describe use of gene expression profiles for diagnosis of oral cancer. Although Warrington et al. disclose about 29 genes listed in Table 1 of the present application, Warrington et al. do **not** teach or suggest step (b) or (c) of claim 1, which involves a test expression profile and a signature expression profile of at least 40 genes selected from SEQ ID NOs: 1-43. In addition, Warrington et al. do **not** teach or suggest step (b) or (c) of new claim 33, which involves a test expression profile and a signature expression profile of at least 5 genes selected from SEQ ID NOs: 3, 5, 10, 15, 16, 21, 22, 27, 28, 31, 32, 35, 37, and 40.

Accordingly, Warrington et al. do not teach all the elements of independent claim 1 or 33 and fail to anticipate claim 1 or 33. For the same reasons, Applicants submit that all claims depending from claim 1 or 33 are not anticipated by Warrington et al. In view of the above amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

CONCLUSION

In view of the above remarks, Applicants believe that the pending application is in condition for allowance. A Petition for a three-month of extension of time and appropriate fees are concurrently filed herewith. If an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. **MIN-P01-042** from which the undersigned is authorized to draw.

Dated: May 28, 2008

Respectfully submitted,

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